

WE CLAIM:

1. An antifibrillrogenic agent for inhibiting amyloidosis and/or for cytoprotection, comprising a peptide selected from the group consisting of penta-, tetra-, and tri- peptides of truncated ANFLVH (SEQ. ID. NO. 11), or an isomer thereof, a retro or a retro-inverso isomer thereof, a peptidomimetic thereof, or a salt thereof.
- 5 2. The antifibrillrogenic agent of claim 1, wherein said peptide is ANFLV (SEQ. ID. NO. 22), ANF (SEQ. ID. NO. 24), or NFL (SEQ. ID. NO. 33), an isomer thereof, a retro or a retro-inverso isomer thereof, a peptidomimetic thereof, or a salt thereof.
- 10 3. The antifibrillrogenic agent of claim 1, wherein the agent comprises a tripeptide selected from the group consisting of ANF (SEQ. ID. NO. 24), ANX (SEQ. ID. NO. 28), AXF (SEQ. ID. NO. 29), and XNF (SEQ. ID. NO. 30), where X is any amino acid except cysteine, or an isomer thereof, a retro or a retro-inverso isomer thereof, a peptidomimetic thereof, or a salt thereof.
- 15 4. The antifibrillrogenic agent of claim 3, wherein the tripeptide is selected from the group consisting of ANF (SEQ. ID. NO. 24), GNF (SEQ. ID. NO. 25), and AGF (SEQ. ID. NO. 26), or an isomer thereof, a retro or a retro-inverso isomer thereof, a peptidomimetic thereof, or a salt thereof.
5. The antifibrillrogenic agent of any one of claims 1 to 4, wherein said agent is an all-[D] isomer of said peptide.
- 20 6. The antifibrillrogenic agent of any one of claims 1 to 4, wherein said agent is an all-[L] isomer of said peptide.
7. The antifibrillrogenic agent of any one of claims 1 to 4, wherein said agent contains a mixture of [L] and [D] isomers of said peptide.
- 25 8. A peptide for inhibiting amyloidosis and/or cytoprotection, said peptide selected from the group consisting of penta-, tetra-, and tri- peptides of truncated ANFLVH (SEQ. ID. NO. 11), or an isomer thereof, a retro or a retro-inverso isomer thereof, a peptidomimetic thereof, or a salt thereof.
9. The peptide of claim 8, wherein said peptide is ANFLV (SEQ. ID. NO. 22) or ANF (SEQ. ID. NO. 24).
- 30 10. The peptide of claim 8, wherein said peptide is a tripeptide selected from the group consisting of ANF (SEQ. ID. NO. 24), ANX (SEQ. ID. NO. 28), AXF (SEQ. ID. NO. 29), and XNF (SEQ. ID. NO. 30), where X is any amino acid except cysteine, or an isomer thereof, a retro or a retro-inverso isomer thereof, a peptidomimetic thereof, or a salt thereof.
11. The peptide of claim 10, wherein the peptide is selected from the group consisting of ANF (SEQ. ID. NO. 24), GNF (SEQ. ID. NO. 25), and AGF (SEQ. ID. NO. 26), or an isomer thereof, a retro or a retro-inverso isomer thereof, a peptidomimetic thereof, or a salt thereof.
- 35 12. The peptide of claim 11, wherein said sequence is ANF (SEQ. ID. NO. 24).
13. The tripeptide of claim 10, wherein said amyloidosis is IAPP-related.
14. The tripeptide of claim 10, wherein said amyloidosis is type 1 or type 2 diabetes.

15. A composition for inhibiting amyloidosis and/or for cytoprotection, comprising a therapeutically-effective amount of the peptide of claim 8 in association with a pharmaceutically-acceptable carrier.

16. A composition for inhibiting amyloidosis and/or for cytoprotection, comprising a therapeutically-effective amount of the peptide of any one of claims 9-11 in association with a pharmaceutically-acceptable carrier.

5 17. A compound for inhibiting amyloidosis and/or for cytoprotection, wherein said compound binds with the peptide of claim 8.

18. The compound of claim 17, wherein said compound is an enzyme that binds to or controls the expression of the peptide.

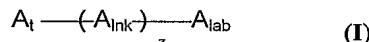
10 19. The compound of claim 17, wherein said compound is an antibody that binds to the peptide.

20. The compound of claim 19, wherein said antibody specifically binds to the peptide.

21. The compound of claim 20, wherein said antibody is a monoclonal antibody.

22. The compound of claim 17, wherein said compound is a salt.

15 23. A labeled conjugate for *in vivo* imaging of amyloid deposits, comprising a conjugate of formula I:



where z is 0 or 1; A_t is the antifibrillrogenic agent of any one of claims 1 to 7; A_{ink} is a linker moiety; and A_{lab} is a labeling moiety that allows for said *in vivo* imaging.

20 24. The labeled conjugate of claim 23, wherein said agent is an all-[D] isomer peptide.

25. The labeled conjugate of claim 23, wherein said agent is an all-[L] isomer peptide.

26. The labeled conjugate of claim 23, wherein A_{lab} is a radiolabeling moiety.

27. The labeled conjugate of claim 26, wherein A_{lab} is selected from the group consisting of ^{99m}Tc , ^{99}Tc , ^{64}Cu , ^{67}Cu , ^{97}Ru , ^{119}Pd , ^{186}Re , ^{188}Re , ^{111}In , ^{113m}In , ^{153}Gd , ^{90}Y , ^{153}Sm , ^{166}Ho , ^{198}Au , ^{90}Sr , ^{89}Sr , ^{115}Rh , ^{201}TI , ^{51}Cr , ^{67}Ga , ^{57}Co , ^{60}Co , ^{123}I , ^{125}I , ^{131}I , and ^{18}F .

28. The labeled conjugate of claim 23, wherein said amyloid deposits comprise IAPP amyloid.

29. The labeled conjugate of claim 23, wherein said amyloid deposits are associated with type 1 or type 2 diabetes.

30. A composition for *in vivo* imaging of amyloid deposits, comprising a therapeutically-effective amount of the labeled conjugate of claim 23, and a pharmaceutically-acceptable carrier.

31. A composition for the treatment of amyloidosis disorders in a patient, comprising a therapeutically-effective amount of the labeled conjugate of claim 23, and a pharmaceutically-acceptable carrier.

32. A method for the treatment of amyloidosis disorders in a patient, comprising administering to said patient a therapeutically-effective amount of the antifibrillrogenic agent of any one of claims 1 to 7.

35 33. The method of claim 32, wherein said amyloidosis disorder is IAPP-related.

34. The method of claim 33, wherein said amyloidosis disorder is type 1 or type 2 diabetes.

35. The method of claim 34, wherein said antifibrillogenic agent is administered in conjunction with another agent selected from the group consisting of insulin, sulfonylurea, and glucose sensitizers.
36. A method for the treatment of amyloidosis disorders in a patient, comprising administering to said patient a therapeutically-effective amount of the composition of claim 31.
- 5 37. The method of claim 36, wherein said amyloidosis disorder is IAPP-related.
38. The method of claim 37, wherein said amyloidosis disorder is type 1 or type 2 diabetes.
39. The method of claim 37, wherein said composition is administered in conjunction with another agent selected from the group consisting of insulin, sulfonylurea, and glucose sensitizers.
- 10 40. A process for the preparation of cells suitable for transplantation into a mammal, which cells are capable of forming amyloid deposits, said process comprising contacting cells *in vitro* with the antifibrillogenic agent of any one of claims 1 to 7 for inhibiting amyloid deposit formation.
41. The process of claim 40, wherein said antifibrillogenic agent causes breakdown of amyloid deposits, the deposits having been formed by said cells prior to said contact.
- 15 42. The process of claim 40, wherein said cells are cultured in the presence of said antifibrillogenic agent.
43. The process of claim 40, wherein said amyloid deposits comprise IAPP amyloid.
44. The process of claim 40, wherein said amyloid deposits are associated with type 1 or type 2 diabetes.
- 20 45. The process of claim 40, wherein said cells, prior to treatment, form amyloid deposits.
46. Cells suitable for transplantation into a mammal, which have been prepared by the process of claim 40.
47. A method for treating a type 1 or type 2 diabetes patient after transplantation, said method comprising the step of administering *in vivo* to said patient the antifibrillogenic agent of any one of claims 1 to 7 for inhibiting, preventing, and/or reducing amyloid deposit formation and amyloidosis.
- 25 48. The method of claim 47, wherein said amyloid deposit formation and/or amyloidosis is IAPP-related.
49. The method of claim 47, wherein said composition is administered in conjunction with another agent selected from the group consisting of insulin, sulfonylurea, and glucose sensitizers.
- 30 50. A method for inhibiting amyloidosis and/or for cytoprotection, comprising administering to a subject a therapeutically-effective amount of the antifibrillogenic agent of any one of claims 1 to 7, wherein said antifibrillogenic agent prevents or reduces amyloid deposition.
51. The method of claim 50, wherein said antifibrillogenic agent is administered by cell therapy or gene therapy, wherein cells have been modified to produce and secrete the antifibrillogenic agent.
- 35 52. The method of claim 51, wherein said cells have been modified *ex vivo*.
53. The method of claim 51, wherein said cells have been modified *in vivo*.
54. The method of claim 50, wherein said amyloidosis or amyloid deposition is IAPP-related.

55. The method of claim 50, wherein said amyloidosis or amyloid deposition is type 1 or type 2 diabetes.
56. The method of claim 50, wherein said antifibrillogenic agent is administered in conjunction with another agent selected from the group consisting of insulin, sulfonylurea, and glucose sensitizers.
- 5 57. A method for identifying an optimized peptide for inhibition of amyloidosis, comprising the steps of:
 - (a) choosing an original peptide selected from the group consisting of ANF (SEQ. ID. NO. 24), GNF (SEQ. ID. NO. 25), AGF (SEQ. ID. NO. 26), and NFL (SEQ. ID. NO. 33),
 - 10 (b) systematically substituting at each residue a different amino acid,
 - (c) testing the ability of each derivative to inhibit amyloid fibril formation, and
 - (d) comparing the inhibition of each derivative with the inhibition of the original peptide, wherein an increase in inhibition of the derivative as compared with the original peptide indicates an optimized peptide.
- 15 58. The method of claim 57, wherein the different amino acid is chosen from the group consisting of Gly, Ala, Val, Leu, Ile, Ser, Thr, Met, Asp, Asn, Glu, Gln, Arg, Lys, His, Phe, Tyr, Trp, and Pro.
59. The method of claim 57, wherein the original peptide is ANF (SEQ. ID. NO. 24).
60. The method of claim 57, wherein the testing for inhibition comprises at least one *in vitro* assay system selected from the group consisting of CD, EM, and cell toxicity.
- 20 61. The optimized peptide identified using the method of claim 57.